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EXAMINER

BEISNER, WILLIAM H

ART UNIT	PAPER NUMBER
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1744

DATE MAILED: 01/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/922,013

Applicant(s)

RUTENBERG ET AL.

Examiner

William H. Beisner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2003.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15, 18-20, 24 and 26-29 is/are pending in the application.
- 4a) Of the above claim(s) 1-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-20, 24 and 26-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Claims 1-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/11/2001.

2. This application contains claims 1-15 drawn to an invention nonelected with traverse in the reply filed on 12/11/2001. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Specification

3. The disclosure is objected to because of the following informalities:

The instant specification includes references to copending applications that have issued as U.S. Patents. It is requested that applicants update the references in the instant specification to include the related patent numbers.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 18-20, 24 and 26-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 28, reference to the "brush means" as "having sufficient stiffness" is indefinite. What structure of the brush means has sufficient stiffness. If applicants are intending to invoke 35 USC 112, sixth paragraph, inclusion of this structural language in the means plus function language would provide additional structure to perform the recited function which is not proper when reciting a claim limitation to be encompassed by 35 USC 112, sixth paragraph.

With respect to claim 27, it is not clear how the language of this claim further limits the structure of the device recited in claim 28. While the language may be more specific it is not clear how this claim language further limits the structure of the system which is encompassed by an analytical or imaging apparatus which already is capable of morphological and DNA ploidy analysis of a cell sample. The instant claim language of these claims appears to be a method step and not a clearly defined structural limitation.

With respect to claim 29, use of the language "most suspect atypical cells" is indefinite. The term "most suspect" in claim 29 is a relative term which renders the claim indefinite. The term "most suspect" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

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1. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 24, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Lonky et al.(US 6,258,044).

The reference of Lee et al. discloses a system (500) for detecting precancerous and cancerous cells in a cell population. The system includes an analytical apparatus including imaging (502) and image processing (536). The imaging and image processing components morphologically select individual atypical (abnormal) cells from the cell population (See classifiers 92, 94, and 96 in Figure 4A). Note the reference discloses that at any stage, objects that are classified as normal or artifact are not classified further (See column 10, lines 54-56).

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After passing through stage 1, 2 and 3, abnormal (atypical) cells are further classified a means to conduct DNA ploidy quantization of the selected atypical cells (See ploidy classifier 100).

With respect to claim 28, while the reference of Lee et al. discloses a PAP smear-type of analysis, the reference does not disclose the use of a sample collection brush with the system.

The reference of Lonky et al. discloses that the use of a brush means to collect a cell population for cytological analysis is well known in the art (See brush means, 20). The reference of Lonky et al. discloses that the disclosed brush is capable of collecting cell samples from epithelial tissue having an uppermost surface and tissue containing areas below the uppermost surface (See the abstract and entire disclosure).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the PAP smear to be used in the system of the primary reference using the sampling brush of the reference of Lonky et al. for the known and expected result of providing a means recognized in the art for preparing a cell sample specimen. The brush of Lonky et al. provides the advantage that it allows collected samples to include cells in addition to spontaneously exfoliated cells (See column 4, lines 5-25 and column 4, lines 44-54).

With respect to claim 24, the brush disclosed by Lonky et al. removes cells from at least two layers of epithelial tissue.

With respect to claim 29, in the absence of further positively recited claim language, the three stage classification of the reference of Lee et al. is considered to meet the “most suspect” limitation of claim 29 since it employs a three-stage process for detecting abnormal cells.

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4. Claims 18 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Lonky et al.(US 6,258,044) and Rutenberg et al.(US 5,740,270).

The combination of the references of Lee et al. and Lonky et al. has been discussed above.

Claim 18 differs by reciting that the locations of the atypical cells are retrieved by the analytical apparatus for cell-by-cell analysis.

The reference of Rutenberg et al. discloses a system for classification of cells in a cell sample that employs image processing which is similar to that of the primary reference of Lee et al. The reference of Rutenberg et al. discloses that the locations of the cells which are selected as atypical by the primary and secondary classifiers are stored in the computer system (20) such that tertiary classification can be performed by a person trained to detect truly abnormal cells (See column 8, lines 35-60).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the system of the modified primary reference with a tertiary classification means as taught by Rutenberg et al. for the known and expected result of allowing a person trained to detect abnormal cells can confirm the results of the automated classification system.

5. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Lonky et al.(US 6,258,044), Rutenberg et al.(US 5,740,270) and Bacus (US 5,526,258).

The combination of the references of Lee et al., Lonky et al. and Rutenberg et al. has been discussed above.

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The above claim differs by reciting that the computer plots a histogram to show DNA ploidy.

The reference of Bacus discloses that when using a computer to perform DNA ploidy, it is conventional in the art to employ histograms to show DNA ploidy of selected cells (See Figures 3-6 and 12).

In view of this teaching, when performing DNA ploidy analysis, it would have been obvious to one of ordinary skill in the art to program the computer so as to display the results in the form of histograms for the known and expected result of providing a conventional means in the art to display DNA ploidy information which has been determined by a computer. This provides a visual indication of ploidy for the operator of the automated system.

6. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Lonky et al.(US 6,258,044), Rutenberg et al.(US 5,740,270) and Lee et al.(US 5,787,189).

The combination of the references of Lee et al., Lonky et al. and Rutenberg et al. has been discussed above.

Claim 20 differs by selecting atypical cells using reference cells chosen from the same population.

The reference of Lee et al. ('189) discloses that in an automated cell analysis and imaging system, it is known to employ a reference cell classifier which employs reference cells from the population of cells to be classified and employs the reference cells data when determining atypical cells (See column 4, lines 20-26 and column 5, lines 20-29).

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In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a reference cell classifier in the system of the modified primary reference for the known and expected result of providing a means recognized in the art for compensating for differences in slide preparation (See column 1, lines 12-34).

7. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Lonky et al.(US 6,258,044) and Hemstreet, III et al.(US 5,733,721).

The combination of the references of Lee et al. and Lonky et al. has been discussed above.

The above claim differs by reciting that the system further includes the use of molecular diagnostic techniques on the atypical cells.

The reference of Hemstreet, III et al. discloses that it is known in the art to employ molecular diagnostic techniques when screening cell samples for cancer. See the entire disclosure. The reference discloses that morphological and ploidy analysis techniques can provide abnormal cells which are not cancerous (See column 2, lines 1-16).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to supplement the classification processes of the modified primary reference using a molecular diagnostic technique disclosed by the reference of Hemstreet, III et al. for the known and expected result of providing an additional level of confirmation of cancerous or precancerous cells since morphological and ploidy techniques are capable of indicating abnormal cells which are not precancerous or cancerous.

Response to Arguments

8. Applicant's arguments filed 11/10/2003 have been fully considered but they are not persuasive.

With respect to the 35 USC 112, second paragraph, rejections of record, Applicants comment that claim 23 has been cancelled while claims 27 and 29 have been amended to respond to the rejection.

With respect to claim 27, claim 27 has not been amended as recited by applicants and applicants' comments fail to set forth while the current claim language of claim 27 is considered to be definite.

With respect to claim 29, while claim 29 has been amended, it is not clear how the amendment and/or associated comments clarify the term "most suspect".

With respect to the 35 USC 103 rejections of record over the reference of Lee et al.(US 6,137,899), Applicants argue that claim 28 has been amended to include the claim limitation that the cells to be analyzed exist in epithelial tissue with an uppermost surface and a tissue area below the uppermost surface and the brush means has sufficient stiffness to reach the uppermost surface and area below the uppermost surface. Applicants stress that the sampling brush is materially different from the PAP-type brush of the prior art. Applicants point out that the reference of Lee does not show or suggest the use of such a brush. Applicants finally argue that the additional prior art does not suggest or disclose such a brush.

In response, while the reference of Lee et al. alone does not disclose the claimed brush, the Examiner is of the position that the combination of the references of Lee et al. and Lonky et al. suggest the invention as encompassed by claim 28. The brush disclosed by Lonky et al. is

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structurally the same as the brush recited in claim 28 and the disclosure of Lonky et al. provides motivation for the combination of the use of the brush of Lonky et al. with the system of Lee et al. Note Applicants' comments fail to specifically address the disclosure of the reference of Lonky et al.

For these reasons, the claims remain rejected over the prior art of record.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 571-272-1281. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



William H. Beisner
Primary Examiner
Art Unit 1744

WHB